15. (twice amended) The method of claim [11] 10, wherein the peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59.

Remarks

The claims are drawn to a molecule mimicking the region of human CD59 which is both species specific (i.e., unique to human) and which binds to C9, thereby inhibiting complement activation mediated by formation of the human C5b-9 complex.

There is an important limitation: the compound must structurally mimick human CD59 amino acid resides 42-58 when these amino acids have the same spatial orientation as when present in the intact molecule. The compound must bind specifically to amino acids 359 to 384 of human C9. This limitation has been added to the independent claim. Support is found for example at page 11, lines 13-14. The chemical structures of claim 11 have been incorporated into claim 10.

Rejection under 35 U.S.C. §112

Claims 10-12, and 16-17 were rejected on the basis that the claimed invention is not clearly enabled nor clearly defined in the application. These rejections are respectfully traversed if applied to the amended claims.

As previously discussed, it is well established law that the claims should be interpreted in view of the specification - in this case, the extensive disclosure in the specification at pages 11 and 13-27, which describes molecules including proteins, antibodies, compounds identified using combinatorial, and compounds identified by rational drug design, using the guidelines provided based on the discovery that one short peptide sequence of human CD59 alone is responsible for the species-specific binding of CD59 to inhibit formation of the C5-b9 complex, using the standard of one skilled in the art.

With computer programs that can be downloaded readily from the internet, and the entire amino acid sequences of the relevant molecules (CD59 and C9) being known, it would be routine to create a three dimensional structure as claimed. The invention resides in knowing which portion of these two structures are critical for **species-specific binding.** .

As the examiner is aware the standard for enablement and clarity is what one of skill in the art, would understand from the claims in view of the specification. Those skilled in the art would learn from the extensive examples that a very small region of human CD59 is responsible for CD59 species-specific role as a complement inhibitor. Indeed, the data at page 47 shows just how specific this role is, since substitution of amino acids to create the structure present in the analogous region of rabbit CD59 destroys the ability of the molecule to inhibit C5b-9 complex formation. The computer programs available at the time of filing provide extensive guidance once the data regarding the exact composition and spatial orientation and alignment provided by applicants has been entered into the program. Moreover, the assays can be used as a final determining factor – since the requirements for inhibition are so stringent, failure to inhibit formation of the human C5b-9 complex can be used as a rapid, simple screen. The requirement of a specific functional activity has been incorporated into the independent claim.

Rejections under 35 U.S.C. §102 or 103

Claims 10-12 and 16-17 were rejected as disclosed by or obvious over U.S. Patent No. 5,550,108 to Sims, et al. Claims 10-12 and 16-17 were also rejected as obvious over

the combination of Sims and Chang, et al., J. Biol. Chem.269(42), 26424-26430 (1994). These rejections are respectfully traversed.

Sims et al. is based on the discovery that CD59 inhibits complement activation, not just hemolysis, and notes that antibodies to C9 can be used to inhibit CD59 activity.

There is no disclosure of what region of CD59 imparts species-specificity. Merely because there may be an antibody which binds to C9 does not mean that it mimicks the region of CD59 which is in issue; in fact, absent making the antibody by immunization with this region, and then screening for efficacy in preventing human CD59 activity, it is extremely unlikely that such an antibody could be obtained. See in particular page 47 in this regard.

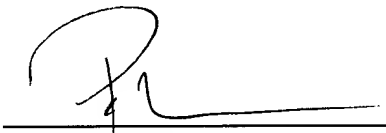
Chang is of no assistance in this regard. Chang identifies the region of human C9 which is bound by human CD59; not the portion of CD59 which binds. One cannot extrapolate from the information relating to human C9 to obtain information about human CD59. The identification of the critical amino acid sequence required careful analysis and many experiments.

In summary, none of the art discloses nor makes obvious the claimed compound which inhibits formation of the human C5b-9 complex, by imitating the structure and function of amino acid residues 42-58.

The requirement for binding to a specific region of C9 is now a specific limitation of the claimed compounds. There is no teaching in the art which discloses nor leads one to this limitation, nor is it obvious. Only through careful, repetitive, and exacting studies was it possible to determine which amino acid residues were critical to block **species specific binding.**

Allowance of all claims 10-19 is earnestly solicited. All claims 10-19 as currently pending are attached in an appendix to facilitate the examiner's review.

Respectfully submitted,



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CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this , along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

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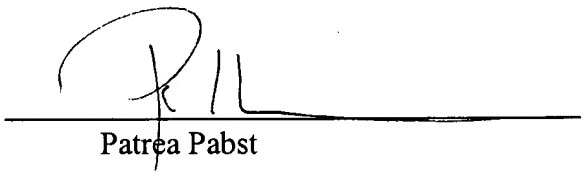

Patrea Pabst

APPENDIX: PENDING CLAIMS 10-19 UPON ENTRY OF AMENDMENT

~~10. (twice amended) A method for inhibiting human C5b-9 complex~~ assembly comprising administering to a patient in need thereof an effective amount of a composition comprising a peptidomimetic selected from the group consisting of proteins, peptides, nucleic acids, and small molecules having the structure and function of human CD59 amino acid residues 42-58, and binding specifically to amino acid residues 359-384 of human C9.

11. (twice amended) The method of claim 10, wherein the peptidomimetic is [selected from the group consisting of proteins, peptides, nucleic acids, and] a small [molecules] molecule which [bind] binds specifically to amino acids 359 to 384 of human C9.

12. (amended) The method of claim [11] 10, wherein the protein is an antibody.

13. (twice amended) The method of claim [11] 10, wherein the protein is a chimeric peptide which includes the amino acids 42 to 58 of the human sequence of CD59.

14. (twice amended) The method of claim [11] 10, wherein the peptide is a covalently cyclized [peptides] peptide comprising human CD59 amino acid residues 42 to 58.

15. (twice amended) The method of claim [11] 10, wherein the peptidomimetic is a peptide of less than forty amino acids residues including amino acid residues 42 to 58 of human CD59.

16. The method of claim 10, wherein the composition further comprises a pharmaceutically acceptable carrier for administration to patients in need thereof.

17. The method of claim 10, wherein the patient is in need of suppression of complement-mediated inflammation.

18. (amended) The method of claim 10 wherein the peptidomimetic comprises the side chains of human CD59 amino acid residues His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the spatial orientation and alignment of hu CD59.

19. (amended) The method of claim 18 wherein the spatial orientation and alignment of the side chains of His^{44}, Asn^{48}, Asp^{49}, Thr^{51}, Thr^{52}, Arg^{55}, and Glu^{58} in the compound are deduced by NMR structure determination.